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EFFECT OF GRAVITATIONAL ACCELERATION, HYPOKINESIA AND HYPODYNAMIA
ON THE STRUCTURE OF THE INTESTINAL VASCULAR BED

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EFFECT OF GRAVITATIONAL ACCELERATION, HYPOKINESIA AND HYPODYNAMIA
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In the numerous studies that have accumulated up till now there are findings /54* of varied morphological changes in the blood vessels of different organs in animals subjected experimentally to hypergravitation (V. I. Stepantsov, 1955; M. G. Prives, 1963; R. A. Bardina, 1964; I. N. Preobrazhenskaya, 1969; V. V. Kupriyanov, 1970; Beckman, 1956; Glasr, Hughes, 1968).

Clinical medicine likewise requires treatment of the question of the effect of mobility restriction on the human organism. Experimental studies in this area distinctly indicate functional and biochemical reorganization in the vascular system of humans and animals, while the findings on morphological changes in the vascular system are still meager and require further thorough investigation (V. A. Odinkova, 1952; L. A. Aleksina, 1968; M. G. Prives, 1970; N. T. Nesterenko, 1973).

Results on the successive effect of gravitational overload and hypokinesia on the vascular system have been presented in individual physiological and morphological studies (V. N. Vinogradov, V. P. Petrukhin, I. V. Fedorov, 1968; V. S. Baybara, 1973; A. A. Kasimtsev, 1973; Miller, Leverett, 1965).

In contrast to other organs the intestine is relatively mobile and easily displaced under all conditions and this fact to a certain degree results in a uniqueness in the changes in this organ when it is affected by various kinds of extreme factors.

The purpose of the present study was to disclose morphological changes in the blood vessels of the small and large intestine of the rabbit under conditions of general hypokinesia and the resulting hypodynamia, of gravitational overload and the combined effect of the factors listed. Material for the study was provided by 110

* Numbers in the margin indicate pagination in the foreign text.

rabbits, of which 8 were used as controls and served for the study of the ordinary structure of the intramural blood vessels of the small and large intestine. In series I the animals (24 rabbits) were put in specially made narrow cages for periods of 1-12 weeks. Animals of series II (21 rabbits) were subjected to single threshold endurable gravitational overloads at 9.6 G in various directions (head-pelvis ($+G_z$), pelvis-head ($-G_z$), chest-back ($+G_x$)) and killed immediately following rotation. In series III the animals (20 rabbits) were subjected to the successive effect of single threshold endurable gravitational overloads in one of the directions listed above and to restricted mobility for periods of 4-16 weeks. In series IV the rabbits (21) were successively subjected to single threshold endurable overloads in one of the directions, to hypokinesia for 4 weeks and then once more to the overloads mentioned. The special feature of series V (in contrast to IV) was prior training of the animals (following special programs) to the first effect of threshold endurable overloads of a significant quantitative and time-related character.

The investigative method comprised injection of the animal's arterial system with a Herot mass (Paris blue on chloroform) with subsequent stratification of the intestinal wall and clearing by the method of A. M. Malygin (1956), injection of a /55 Hauch rentgenocontrast mass using the modification of M. G. Prives and rentgenography of the intestinal areas under study. In addition we also used the noninjection method for disclosing the blood vessels of the submucous base of the small intestine (silver nitrate impregnation by the method of V. V. Kupriyanov) as well as a histological method (Van Gieson staining of sections). Blood vessel width was measured with an MOV-1-15* filar micrometer.

Normally the intramural blood supply of the small and large intestine is made possible by the base intramural arteries -- vasa recta (arteries of the III order) -- of the arcade ramifications of the a. mesenterica anterior and a. mesenterica posterior. The vasa recta which enter the intestinal wall at right angles to the longitudinal axis of the organ (ventral and dorsal) penetrate into the muscular membrane and on reaching the tela submucosa form therein submucous arterial networks taking the form of arteries of gradually decreasing diameter belonging to the III, IV and V orders and of medium (60-40 microns) and small (40-20 microns) caliber and capillary networks of very variable size and shape (Fig. 1).



Fig. 1. Vascular bed of submucous base of normal small intestine. Cleared preparation. Obj. 8, oc. 7



Fig. 2. Normal vascular bed of tela submucosa of small intestine. Arterioles of smooth muscle sphincter at site of ramification. Silver nitrate impregnation. Obj. 20, oc. 10

mural vascular bed. The formation of venous branches occurs variously but basically the positioning of veins of the III and IV order corresponds to that of their arterial analogues and the diameter of these veins is 1.2-1.3 times that of the correspond-

In preparations of the tela submucosa of the small intestine impregnated with silver nitrate there is a clear disclosure of all the components of the microcirculatory bed: arterioles, precapillaries, capillaries, postcapillaries and venules. As a rule an arteriole is attended by two venules and the arterioles themselves show uniform width and distinct contours. At the site of the arterioles' ramification there are sphincters composed of smooth muscle elements (Fig. 2). In the mucosa of the caecum (distal portion) basal capillary networks are formed comprising capillaries of uniform width (7-9 microns). In both the small and large intestine the ^{/56} vascular networks of muscular membrane show a unique rectangular structure and the capillary networks themselves are attenuated (Fig. 3). In this respect our findings agree with those of M. I. Urmanov (1961), V. M. Pichugin (1966), V. Ya. Kamyshev (1972). Among intramural arteries of all calibers one sees a large number of arterial and venous anastomoses laid out in several rows that follow the intestine. In all blood vessels studied the contours were even and distinct; sinuosity of medium caliber arteries (60-40 microns) was characteristic only for arteries of the intestinal muscular membrane.

The Herot mass, which normally shows good transcapillary penetration, made it possible to disclose the venous portion of the intra-



Fig. 3. Vascular bed of muscular membrane of normal small intestine. Cleared prep. Obj. 8, oc. 7



Fig. 4. Same as above after 2 week hypokinesia. Very sinuous and unevenly constricted arteries of medium and small caliber. Cleared prep. Obj. 8, oc. 7

ing arteries.

Series I. Study of the material from animals that had been in general hypokinesia showed, that the greatest changes due to the early hypokinetic periods (1-2 weeks) occur in the blood vessels of the muscular membrane of the small intestine: uneven constriction and severe sinuosity of medium and small caliber arteries, the capillaries and veins of orders VI, V and IV, on the contrary, being dilated (Fig. 4). Analogous changes are observed likewise in the muscular membrane of the large intestine, but these appear at much later periods of mobility restriction (4-8 weeks). At the end of the first week of hypokinesia the mucosa of the small and large intestine shows constricted arteries of the IV and V order and then, with prolonged mobility /57 restriction, dilated vessels of all calibers, which are distinctly revealed at the end of the fourth week of hypokinesia. Here the diameter of the veins is much larger than that of the arteries (1.5 times or more). In the impregnated preparations of the tela submucosa of the rabbit small intestine in animals subjected to hypokinesia for 4 weeks one notices severe sinuosity of the arterioles, microaneurisms of arterioles and varicose dilatation of venules and movement of formed blood elements beyond the confines of the vessels (Fig. 5). There is a dilatation of arteriovenous anastomoses, which appear in relatively larger numbers and this facilitates injection of the venous portion of the intramural vascular bed (this, in our opinion, corroborates the hypothesis of M. I. Urmanov, 1968, on the regulatory

role of arteriovenous anastomoses when there is a change in the hemodynamic conditions



Fig. 5. Vascular bed of tela submucosa of small intestine after 4 week hypokinesia. Unevenly dilated arterioles, movement of formed blood elements out of bed. Silver nitrate impregnation. Obj. 20, oc. 10



Fig. 6. Same after 12 week hypokinesia. Aneurismatic dilation of arteries and arterioles. Cleared preparation. Obj. 20, oc. 7

of the intestinal wall). When the hypokinetic period is 8-12 weeks we find, together with dilated arteries and veins of medium caliber, deformation of the vascular wall (local aneurismatic and varicose protrusions) and exit of the injection mass (Fig. 6). In contrast with the normal (Fig. 7) there is in the histological preparations a definite attenuation of the muscular membrane of the arteries of the tela submucosa of the small intestine and in a number of cases we meet with degenerated muscular fibers. One also notes the growth of the sheath of perivascular connective tissue (Fig. 8). On the basis of the material studied we may conclude, that hypokinesia exerts a marked influence on organs (in this case the intestine), whose smooth musculature continues to carry out its activity despite the presence in the organism of general hypokinetic conditions.

Series II. Following single threshold endurance /58 overloading in the head-pelvis direction ($+G_z$) in the wall of the small intestine (especially in its mucous membrane and tela submucosa) arteries of all calibers appear slightly constricted and capillaries unevenly dilated. Arteries and veins have a sinuous character and their shape is reminiscent of "rosary beads". In the caecum wall one observes evenly dilated arterial and venous vessels. Overload in the caudocranial direction (G_z) produces a significant dilation of all links in the microcirculatory bed of the membranes of the small intestine. One's attention is drawn to the density

of the capillary networks due to the diameter increase of the capillaries that make them up (10-12 microns). It seems that the appearance of highly sinuous arteries of



Fig. 7. Vascular bed of tela submucosa of normal small intestine. Van Gieson. Obj. 20, oc. 10.



Fig. 8. Same after 12 week hypokinesia. Growth of connective tissue around arteries and veins. Van Gieson. Obj. 20, oc. 10.

of all capillaries should be regarded as a defense feature for safeguarding the terminal portion of the vascular bed of the membranes of the small intestine. In the caecum wall under the same conditions the arteries appear relatively constricted. When the load direction is ventrodorsal ($+G_x$) the wall of the areas studied shows marks of pronounced venous stasis (unevenly dilated and sinuous capillaries and veins of all orders; in a number of cases movement of the injected mass beyond the vessel limits).

Series III. The combined successive effect of gravitational overload and hypokinesia covering 4-16 weeks aggravates the picture of morphological changes in the intestinal vascular system. Severely dilated arteries, veins and vessels of the microcirculatory bed appear regardless of the acceleration vector preceding hypokinesia. Destructive changes in the vascular wall (rupture, aneurismatic and varicose dilation) are noted, when there are combinations of extreme /59 factors such that initially the overloads work in a ventrodorsal direction (Fig. 9). The results of this series show, that when extreme effects are combined the changes in the vascular bed of the intestine exhibit a more pronounced character, than is observed when each factor exerts its influence alone. In this context transverse overloads have a relatively greater effect on the character of successive vascular changes

in the wall of the small and large intestine.

Series IV. In this series the animals were kept under conditions of general hypokinesia for 4 weeks between two single threshold endurable gravitational overloads in a given direction. A study of the preparations at the end of the experiment showed



Fig. 9. Vascular bed of tela submucosa of the small intestine after single threshold endurable overloads in the chest-back direction and subsequent hypokinesia (8 weeks). Aneurismatically dilated arteries and seepage of injection mass beyond vascular limits. Cleared preparation. Obj. 8, oc. 10.

the following: in all membranes of the wall of the small intestine of rabbits subjected to rotation in the head-pelvis direction ($+G_z$) there appear constricted arteries of all orders, capillaries constricted unevenly and in places "in bead fashion" and severely dilated arterio-venous anastomoses. In the wall of the large intestine (likewise in all membranes) one notes severely distorted arterial vessels together with dilated arteries and capillaries. Following overload in the direction pelvis-head ($-G_z$) arteries of all calibers in the mucosa of the small intestine are severely di-

lated and sinuous, anastomoses between arteries of all calibers distinctly visible. Vascular changes in the wall of the large intestine are similar to those observed in animals that had been in hypokinesia alone for 4 weeks. In the wall of the small and large intestine of rabbits subjected to chest-back overloads the end of the experiment revealed attenuated vascular networks and constricted arteries of medium and small caliber. The degree of venous congestion was lower than in animals of the previous series. It should be noted, that in the series under discussion the blood vessels of the muscular membrane were less subject to morphological changes occurring as a re- /60
sult of the interaction of extreme factors.

Series V. The results of this series show, that preliminary training of animals for the subsequent effect of single, significantly large threshold endurable gravitational overloads has known positive significance and prepares them for the first effect of hypergravitation, but subsequent maintenance of the animals in 4 weeks hypokinesia results in detraining them to subsequent gravitational overloads (P. M. Suvorov, 1967). The morphological changes in the intestinal vessels of animals in this series fit into the picture of vascular changes that occur only when there is a gravitational overload.

Thus the data obtained in our experiments correspond to a certain extent with the character of general morphological changes occurring in the vascular system when mobility is restricted (M. G. Prives, 1970), despite the fact, that the intestine is not an organ whose movements are restricted under general hypokinesia. All the morphological changes in the wall of the small intestine observed during the early stages of hypokinesia (constricted arteries in the mucous membrane and tela submucosa and dilated vessels in the muscular membrane) may be explained by a redistribution of the blood due to serious functional changes in the working of the small intestine (animals refusing feed, intestinal atonia, disruption of secretion of intestinal fluid). In addition there appear during much later periods of restricted mobility destructive changes in the structure of blood vessel walls (aneurismatic and varicose dilation, wall rupture, escape of injection mass and formed blood elements from the confines of the vessels, degenerated muscular fibers in arterial walls). Analogous vascular changes, but of a more pronounced character, were observed in the skeletal musculature of animals subjected to general hypokinesia (L. A. Aleksina, 1968; Z. A. Saryyeva, 1972). Consequently, we may theorize, that the effect of hypokinesia on the intramural vascular bed of the intestine (and especially of its smooth musculature) exhibits a nonspecific effect and that this effect spreads to the blood vessels of an organ that loses little of its mobility when the organism is in general hypokinesia.

The action of the hypergravitational factor causes ordinary morphological transformations (in response to hemodynamic restructuring) in the vascular system of the intestine, as was shown earlier by M. I. Urmanov (1968, 1969) but these transformations are more pronounced when the overload is in a ventrodorsal direction. When there is successive action by gravitational overload and hypokinesia, what stands out most prominently is the vascular changes attached to the effect of hypokinesia. Repeated gravitational overloading after hypokinesia aggravates the picture of morphological changes in the vascular bed of the intestine but in this context the phenomena allied with overloading are predominant. Prior training of animals to the effect of quantitatively significant threshold endurable gravitational overloads does not exhibit a positive effect on the character of vascular changes following repeated overloading after 4 weeks of hypokinesia.

REFERENCES

1. Aleksina, L. A., Vliyaniye gipodinamii na obrazovaniye kollateral'nykh putey limfootoka [Effect of Hypodynamia on the Formation of Collateral Lymph Pathways], Author's abstract of doctoral cand. dissertation, Leningrad, 1968.
2. Baybara, V. S., Vliyaniye ekstremal'nykh faktorov na mikrotsirkulyatornoye ruslo bronkhov [Effect of Extreme Factors on the Microcirculatory Bed of the Bronchi], Author's abstract of doctoral cand. dissertation, Leningrad, 1973.
3. Bardina, R. A., Ark. anat. 11, 41-44 (1964).
4. Beckman, E. L., J. of Aviation Medicine 29, 2, 117-130 (1956).
5. Glasilr, J. B. and L. M. Hughes, Aerospace Medicine 38, 3, 282-286 (1968).
6. Kamyshev, V. Ya., Sravnitel'naya anatomiya kapillyarov i arterio-venoznykh anastomozov v svyazi s privodyashchim i otvodyashchim zven'yami vnutristenochnykh krovenosnykh sosudov bryzheychnoy chasti sredney kishki pozvonochnykh zhivotnykh i cheloveka [Comparative Anatomy of Capillaries and Arteriovenous Anastomoses in connection with the Afferent and Efferent Links of Intramural Blood Vessels of the Mesenteric Portion of the Middle Intestine in Vertebrate Animals and Man], Author's abstract of doctoral dissertation, Volgograd, 1972.
7. Kasimtsev, A. A., Ark. anat. 2, 82-90 (1973).
8. Kupriyanov, V. V. in the collection: Mekhanizmy vnesosudistoy i intramural'noy regulyatsii krovotoka v patologii i eksperimente [Mechanisms of Extravascular and Intramural Regulation of Blood Flow in Pathology and Experiment], Moscow, 1970, 3, pp 3-13.
9. Malygin, A. M., Azerbaydzhanskiy med. zhurn. 6, 75-77 (1956).
10. Miller, P. B. and S. D. Leverett, Aerospace Medicine 36, 1, 13-16 (1965).
11. Nesterenko, N. T., Ark. anat. 5, 44-50 (1973).
12. Odinkova, V. A., Osobennosti neyroticheskoy atrofii skeletnoy muskulatury v otlicheye ot atrofii ot bezdeystviya [Features of Neurotic Atrophy of Skeletal Musculature as Distinguished from Atrophy due to Immobility], Author's abstract of doctoral candidate's dissertation, Moscow, 1952.
13. Pichugin, V. M., Vnutriorgannyye arterii, kapillyary i veny tonkoy kishki cheloveka i sredney kishki nekotorykh zhivotnykh [Intraorganic Arteries, Capillaries and Veins of the Human Small Intestine and the Middle Intestine of Some Animals], Author's abstract of doctoral candidate's dissertation, Khabarovsk, 1966.
14. Preobrazhenskaya, I. N., Ark. anat. 10, 25-30 (1969).
15. Prives, M. G., Ark. anat. 11, 3-13 (1963); ibid 4, 9-19 (1970).
16. Saryyeva, Z. A., Vliyaniye gipokinezii i gipodinamii na arterial'noye ruslo i

obrazovaniye arterial'nykh kollateral'nykh konechnostey [Effect of Hypokinesia and Hypodynamia on the Arterial Bed and the Formation of Arterial Collaterals in the Pelvic Extremities], Author's abstract of doctoral candidate's dissertation, Leningrad, 1972.

17. Stepantsov, V. I., Vliyaniye peregruzok, deystvuyushchikh v napravlenii golovataz na arterial'noye ruslo myshts bedra [Effect of Overload in the Head-Pelvis Direction on the Arterial Bed of the Pelvic Muscles], Author's abstract of doctoral candidate's dissertation, Leningrad, 1955.
18. Suvorov, P. M., Aviatsiya i kosmonavtika 1, 76-78 (1967).
19. Urmanov, M. I., Vnutriorgannyye arterii, kapillyary i veny tolstoy kishki cheloveka i nekotorykh zhivotnykh [Intraorganic Arteries, Capillaries and Veins of the Large Intestine in Humans and Some Animals], Author's abstract of doctoral candidate's dissertation, Leningrad, 1961 in the collection: Voprosy aviatsionnoy i kosmicheskoy anatomii [Problems of Aviation and Space Medicine], Leningrad, 1968, pp 49-53; Transactions of the VII Congress of Anatomists, Histologists and Embryologists, Tbilisi, 1969, pp 358-359.
20. Vinogradov, V. N., V. G. Petrukhin and I. V. Fedorov, Byull. eksper. biol. i med. 6, 96-99 (1968).